PATENT COOPERATION TREATY

om th	ne NATIONAL SEARC	HING AUTHC	RITY		REC'D U O JUL 2005		
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Г о :							
				WRITT	EN OPINION OF THE		
	see form Po	CT/ISA/220		INTERNATION	AL SEARCHING AUTHORITY		
				(P	CT Rule 43 <i>bis</i> .1)		
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				Date of mailing (day/month/year) see	form PCT/ISA/210 (second sheet)		
Annlie	cant's or agent's file re	eference		FOR FURTHER A	CTION		
	form PCT/ISA/220			See paragraph 2 below	N		
	national application No.		International filing date (da 07.04.2005	ay/month/year)	Priority date (day/month/year) 07.04.2004		
			both national classification a	and IPC			
cnterr	national Patent Classi 2N15/75, C12N1/2	1					
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	icant VOZYMES A/S						
1.	This opinion co	ntains indicat	ions relating to the follo	owing items:	•		
••		Basis of the o					
	Box No. I Box No. II	Priority	pinion	·			
	Box No. III	Non-establish	ment of opinion with rega	ard to novelty, inventiv	ve step and industrial applicability		
	Box No. IV	Lack of unity	of invention				
	Box No. V	Passanad sta	atement under Rule 43 <i>bis</i> citations and explanations	s.1(a)(i) with regard to s supporting such stat	novelty, inventive step or industrial terment		
	☐ Box No. VI	Certain docui					
	☐ Box.No. VII	Certain defec	ts in the international app	olication	•		
	図 Box No. VIII		rvations on the internation				
2.	FURTHER ACT	ION	-		<u>-</u>		
•	written opinion of the applicant cho International But will not be so co	of the Internation ooses an Authoreau under Rub Insidered.	onal Preliminary Examining ority other than this one to le 66.1 bis(b) that written o	o be the IPEA and the opinions of this intern	Il usually be considered to be a However, this does not apply where chosen IPEA has notifed the ational Searching Authority		
	If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is Invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.						
	For further options, see Form PCT/ISA/220.						
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Na	ame and mailing addr	ess of the ISA:		Authorized Officer	Suck Es Polonians.		
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	NL-2280	HV Rijswijk - Pa	P.B. 5818 Patentlaan 2 ys Bas k: 31 651 epo nl	Montero Lopez,	B ()		

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/DK2005/000236

	Box	x No	. I Basis of the opinion			
1.	Wit the	h reg lang	gard to the language, this opinion has been established on the basis of the international application in juage in which it was filed, unless otherwise indicated under this item.			
		lan	s opinion has been established on the basis of a translation from the original language into the following guage , which is the language of a translation furnished for the purposes of international search der Rules 12.3 and 23.1(b)).			
2.	Wit nec	With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:				
	a. t	ype	of material:			
	į	\boxtimes	a sequence listing			
			table(s) related to the sequence listing			
,	b. f	orm	at of material:			
		\boxtimes	in written format			
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	c. t	ime	of filing/furnishing:			
•		\boxtimes	contained in the international application as filed.			
		\boxtimes	filed together with the international application in computer readable form.			
			furnished subsequently to this Authority for the purposes of search.			
3.		ha: co _l	addition, in the case that more than one version or copy of a sequence listing and/or table relating theretos been filed or furnished, the required statements that the information in the subsequent or additional pies is identical to that in the application as filed or does not go beyond the application as filed, as poropriate, were furnished.			
4.	Add	ditio	nal comments:			
	Во	x No	o. VIII Certain observations on the international application			

see separate sheet

Form PCT/ISA/237 (January 2004)

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

- D1: KYOKO KANAMARU ET AL.: "Overexpression of the PepF oligopeptidase inhibits sporulation initiation in Bacillus subtilis" JOURNAL OF BACTERIOLOGY, vol. 184, no. 1, January 2002 (2002-01), pages 43-50, XP002334436
- 1. The present application relates to the production of heterologous proteins in Bacillus cells which have been mutated to reduce the expression-levels of the YusZ or YusX genes.
- 2. Document D1 discloses that B. subtilis YusX gene encode an oligoendopeptidase and that YusX and YusY may be a single ORF. The function of the YusXY protein appears to be unknown. There is no hint in the state of the art to indicate the skilled person that reduced expression of YusX or YusZ in Bacillus would improve secretion of heterologous proteins. Claims 1-57 therefore are novel and inventive and comply with the requirements of Articles 33(2) and (3) PCT.

Re Item VIII

Certain observations on the international application

- 1. Claims 1, 5, 6, 20, 25, 39 and 44 include the sequence of the Yus protein or polynucleotide between parenthesis. This renders the sequence an optional feature which does not have any limiting effect in the scope of the claims. The deletion of the parenthesis and specification of the sequence would improve the clarity of the claims as requested according to Article 6 PCT.
- 2. The relative term "homologue" used in claims 1, 5-8, 10-13, 20, 24-27, 29-32, 39, 43-46, 48, 50 and 51 has no well-recognised meaning and leaves the reader in doubt as to the

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

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PCT/DK2005/000236

meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT). It is unclear what sort of homology (functional, structural) is meant and what the degree of homology should be.

- 3. The relative term "polypeptide of interest" used in claims 1, 20 and 39 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).
- 4. The feature of claims 6-11, 25-30 and 44-49 of a mutation in the YusY gene is not supported by the examples. The examples show only the expected effect for YusX and YusZ deletion mutants. Claims 6-11, 25-30 and 44-49 are therefore not supported by the description as required by Article 6 PCT.
- 5. Claims 19, 38 and 57 include an optional feature (preferably derived from the Cryllla promoter) which does not have any limiting effect in the scope of the claims. The deletion of this feature would improve the clarity of the claims as requested according to Article 6 PCT.

PATENT COOPERATION TREATY

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		Date of mailing (day/month/year) s	ee form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220		FOR FURTHER See paragraph 2 be	
International application No. PCT/DK2005/000236	International filing date (07.04.2005	day/month/year)	Priority date (day/month/year) 07.04.2004
International Patent Classification (IPC) or to C12N15/75, C12N1/21	ooth national classification	and IPC	
		<u>,</u>	·
Applicant NOVOZYMES A/S	•		
1. This opinion contains indication Box No. I Basis of the op		llowing items:	· •
☐ Box No. II Priority			
☐ Box No. III Non-establishr	ment of opinion with reg	gard to novelty, inver	ntive step and industrial applicability
Box No. IV Lack of unity of	f invention	·	
☐ Box No. V Reasoned stat applicability; ci	tement under Rule 43b itations and explanation	is.1(a)(i) with regard as supporting such st	to novelty, inventive step or industrial tatement
☐ Box No. VI Certain docum			
	s in the international ap		·
🛛 Box No. VIII Certain observ	rations on the internation	onal application	
2. FURTHER ACTION			
written opinion of the Internation the applicant chooses an Author International Bureau under Rule will not be so considered.	nal Preliminary Examini rity other than this one e 66.1 <i>bis</i> (b) that written	ng Authority ("IPEA") to be the IPEA and the opinions of this inter	mational Searching Authority
- when it to the IDEA a written ren	ly together where app	ropriate, with amend:	ne IPEA, the applicant is invited to ments, before the expiration of three on of 22 months from the priority date,
For further options, see Form Po	CT/ISA/220.		•
3. For further details, see notes to	Form PCT/ISA/220.		
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Name and mailing address of the ISA:		Authorized Officer	nes Polonia.

Montero Lopez, B

Telephone No. +31 70 340-3739

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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International application No. PCT/DK2005/000236

has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. 4. Additional comments: Box No. VIII Certain observations on the international application						
the language in which it was filed, unless otherwise indicated under this item. This opinion has been established on the basis of a translation from the original language into the followin language which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)). With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of: a type of material: a sequence listing table(s) related to the sequence listing b. format of material: in written format in computer readable form c. time of filing/furnishing: contained in the international application as filed. filed together with the international application in computer readable form. furnished subsequently to this Authority for the purposes of search. In addition, in the case that more than one version or copy of a sequence listing and/or table relating there has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. Additional comments:		Box N	lo. I Basis of the opinion			
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The following shape of the same that the sam	TL -	· falls:	ving observations on the clarity of the claims, description, and drawings or on the question whether the			

Form PCT/ISA/237 (January 2004)

see separate sheet

PCT/DK2005/000236

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